UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,282	07/08/2003	Dung-Fang Lee	8842.0001	2568

22852 7590 07/15/2005

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,282	LEE ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12-14,17,20-26 and 40-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12-14,17,20-26 and 40-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the First Action was filed on March 18, 2005. Applicant filed a supplemental response on April 26, 2005. Claims 6-11, 15-16, 18-19 and 27-35 are cancelled. Claims 36-39 are withdrawn. Claims 40-53 are newly added. Claims 17, 23, 36-39 are amended.

Claims 1-5, 12-14, 17, 20-26, and 40-53 are under consideration.

It is noted that while there had been a species election to six distinct viral vectors (page 3 of the Restriction Requirement, September 22, 2004), and the Applicant had elected baculovirus in the Response to the Restriction Requirement (October 18, 2004), the Examiner is now considering all six viral vectors. The reason for this is because the six vectors are used as a vehicle to deliver the claimed invention.

Withdrawn Rejections

Rejections under 35 U.S.C. §112, first paragraph, Enablement

Deposit Requirement

The rejection of claims 1-5, 12-14, 17, and 20-26 regarding a deposit requirement is withdrawn. Applicant's arguments, see pages 11-12 of the Applicant's response, filed March 18, 2005, with respect to claims 1-35 have been fully considered and are persuasive.

Promoter

The rejection of claims 1-5, 12-14, and 17 regarding a "promoter" is withdrawn. Applicant's arguments, see pages 12-15 of the Applicant's response, filed March 18, 2005, with respect to claims 1-5, 12-14, and 17 have been fully considered and are persuasive.

Homolog

The rejection of claims 1-5, 12-14 regarding a "homolog" is withdrawn. Applicant has amended the claims.

Host cells comprising vectors

The rejection of claims 12-14 regarding a "host cell comprising a nucleic acid vector" is withdrawn. Applicant's arguments, see page 19 of the Applicant's response, filed March 18, 2005, with respect to claims 12-14 have been fully considered and are persuasive.

Rejections under 35 U.S.C. §112, first paragraph, Written Description

Promoter

The rejection of claims 1-5, 12-14, and 17 regarding a "promoter" is withdrawn. Applicant's arguments, see pages 20-21 of the Applicant's response, filed March 18, 2005, with respect to claims 1-5, 12-14, and 17 have been fully considered and are persuasive.

New and Maintained Rejections

Rejection under 35 U.S.C. § 112, first paragraph, Enablement

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection for claims 1-5, 12-14, 17, 20-26, and 53 for scope of enablement is maintained under 35 U.S.C. 112, first paragraph, for reasons of record (December 21, 2004), because the specification, while being enabling for

a recombinant nucleic acid vector encoding a nucleic acid sequence comprising at least two cistrons and at least one nucleotide sequence that provides IRES activity operably linked to at least one of said at least two cistrons, wherein the nucleotide sequence that provides IRES activity comprises a nucleotide sequence selected from the group consisting of:

a) a nucleotide sequence of SEQ ID NO.1;

b) a nucleotide sequence of nucleotides 1-215 of SEQ ID NO. 1;

c) a nucleotide sequence of nucleotides 45-239 of SEQ ID NO. 1;

d) a nucleotide sequence of nucleotides 45-215 of SEQ ID NO. 1;

e) a nucleotide sequence of nucleotides 1-74 and 187-239 of SEQ ID NO. 1;

f) a nucleotide sequence of nucleotides 1-74 and 187-215 of SEQ ID NO. 1;

g) a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 1 by substitution of the nucleotides at positions 124-127 of SEQ ID NO. 1;

h) a nucleotide sequence of SEQ ID NO. 2;

i) a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 2 by substitution of the nucleotides at positions 136-139 of SEQ ID NO. 2

does not reasonably provide enablement for

a nucleic acid vector for the expression of at least two cistrons comprising

a) a promoter operably linked to a nucleotide sequence comprising at least two cistrons; and

b) at least one nucleotide sequence comprising SEQ ID NO. 1, or a variant or fragment thereof operably linked to at least one of said at least two cistrons, wherein said nucleotide sequence comprises SEQ ID NO. 1, or a variant or fragment thereof, provides IRES activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Variant and Fragment

While Applicant has provided an argument regarding the use of "variant" or "fragment" in claims 1-5, 12-14, 17, and 20-26 on page 18 and 21-23 of the Applicant's response filed March 18, 2005, the argument is moot as the Examiner did not clearly indicate the problem at hand with using the terminology, "variant" and "fragment." It is noted that while Applicant had indicated on page 10-11 of the Applicant's supplemental

response filed April 26, 2005, that the term "variant" had been removed from the claims. However, the claims, as filed on April 26, 2005, had not removed the term "variant."

The enablement problem at hand with using the terms "variant" and "fragment" in the claims is that while the specification provides some definitions and examples of what is meant by "variant" and "fragment" (specification, pages 13-16, 36-38, Table 2, and Figures 6A and B), the specification does not provide guidance such that an artisan can take the teachings of the specification and apply them to other situations and arrive at the claimed invention. The specification teaches that the Drosophila labial IRES has a certain structure (specification, Figure 1B). The specification also teaches that the Drosophila labial IRES can be divided into three domains. It is understood from Figure 1B that each hairpin structure is a domain. The specification teaches that deletion of domains I and part of domain II (deletion of bases 75-186 of the labial IRES) results in dramatic reduction in IRES activity (specification, Table 2). The deletion of domain III results in an increase in IRES-dependent translation (specification, Table 2). While the specification teaches these embodiments about the Drosophila labial IRES, nothing in the specification teaches how to apply the teachings of the deletion studies to the human Homeobox A IRES. One indication that an artisan cannot readily apply the teachings of the labial deletion studies (Table 2) to that of the human Homeobox A IRES sequence is that there is a 70% similarity and a 40% identity between the two sequences. A second indication is that the structures of the two IRESes look different that it is not readily apparent how one could demarcate what in the human Homeobox A IRES is domain I, II, and III (Figures 1B and 4B). Nothing in the specification provides

guidance that it is because of certain regions in the Drosophila IRES or certain positions of nucleic acids within the Drosophila IRES structure that need to be conserved, in order for the activity to be conserved in the human IRES sequence. As such, because the specification does not provide this guidance, an artisan does not know how to make any changes in SEQ ID NO. 1 and SEQ ID NO. 2 such that an artisan can predict that the changes made will result in certain, predictable changes in IRES activity. It should be made clear that the issue is not so much that removing and changing 10-20% of the bases of SEQ ID NO. 1 is the problem of enablement, as the specification shows that even large deletions of domain 2 results in some IRES activity. The focus of the enablement rejection is that the specification does not provide guidance for an artisan to apply the teachings of the specification such that an artisan can arrive the claimed invention for the broad scope of labial IRES and its homologs.

Therefore, while the specification provides enablement for:

a) a nucleotide sequence of SEQ ID NO.1;

b) a nucleotide sequence of nucleotides 1-215 of SEQ ID NO. 1;

c) a nucleotide sequence of nucleotides 45-239 of SEQ ID NO. 1;

d) a nucleotide sequence of nucleotides 45-215 of SEQ ID NO. 1;

e) a nucleotide sequence of nucleotides 1-74 and 187-239 of SEQ ID NO. 1;

f) a nucleotide sequence of nucleotides 1-74 and 187-215 of SEQ ID NO. 1;

g) a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 1 by substitution of the nucleotides at positions 124-127 of SEQ ID NO. 1;

h) a nucleotide sequence of SEQ ID NO. 2;

i) a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 2 by substitution of the nucleotides at positions 136-139 of SEQ ID NO. 2,

the specification does not provide enablement for any homolog, variant, fragment, or sequence at least 80 or 90% identical to SEQ ID NO. 1 commensurate with the scope of the claims.

Claims 1-5, 12-14, 17, 20-26, and 40-53 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a nucleic acid vector for the expression of at least two cistrons comprising:

a promoter operably linked to a nucleotide sequence comprising at least two cistrons, wherein each cistron subsequent to the first cistron is operably linked to an IRES, wherein at least one of the IRESes is the nucleic acid sequence of SEQ ID NO. 1, the nucleotide sequence of nucleotides 1-215 of SEQ ID NO. 1, a nucleotide sequence of nucleotides 45-239 of SEQ ID NO. 1, a nucleotide sequence of nucleotides 45-215 of SEQ ID NO. 1, a nucleotide sequence of nucleotides 1-74 and 187-239 of SEQ ID NO. 1, a nucleotide sequence of nucleotides 1-74 and 187-215 of SEQ ID NO. 1, a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 1 by substitution of the nucleotides at positions 124-127 of SEQ ID NO. 1, a nucleotide sequence of SEQ ID NO. 1, and a nucleotide sequence that differs from a nucleotide sequence comprising SEQ ID NO. 2 by substitution of the nucleotides at positions 136-139 of SEQ ID NO. 2

does not reasonably provide enablement for

a nucleic acid vector for the expression of at least two cistrons comprising:

a) a promoter perably linked to a nucleotide sequence comprising at least two cistrons, and

b) at least one nucleotide sequence comprising SEQ ID NO. 1, or a variant or fragment thereof operably linked to at least one of said at least two cistrons, wherein said nucleotide sequence comprising SEQ ID NO. 1 or variant or fragment thereof, provides IRES activity.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state

of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claimed invention broadly encompasses expression of at least two cistrons wherein the promoter is operably linked to a nucleotide sequence comprising at least two cistrons and the IRES is operably linked to at least one of the at least two cistrons. The claimed invention broadly encompasses any arrangement of IRES and cistrons. While it is understood from the specification that the intended arrangement of IRES, cistrons, and promoter is: promoter-cistron1-IRES-cistron2, the claims as written also encompass the arrangements of: promoter-IRES-cistron1-cistron2 and promoter-cistron1-cistron2-IRES-cistron3. While the claims embody these other constructs, the specification does not teach how to use them. In the arrangements of: promoter-IRES-cistron1-cistron2 and promoter-cistron1-cistron2-IRES-cistron3, cistron2 would not be translated. Nothing in the specification teaches how an artisan can use either arrangement to obtain a nucleic acid sequence comprising multiple cistrons and to be able to translate all cistrons. It would be undue experimentation for an artisan to practice the claimed invention using the arrangement of: promoter-IRES-cistron1-cistron2 and promoter-cistron1-cistron2-IRES-cistron3 as nothing in the art or the specification provide guidance as to how cistron2 can be expressed in either arrangement.

Therefore, for the reasons described above, the claimed invention is not enabled for its full scope.

Rejection under 35 U.S.C. § 112, first paragraph, Written Description

Claims 1-5, 12-14, 17, 20-26, and 53 are maintained under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/current.html).

The written description requirement for a claimed genus is satisfied by sufficient description of a representative number of species by actual reduction to practice and by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant were in possession of the claimed genus.

Similar to the enablement rejection described above, the written description rejection of claims 1-5, 12-14, 17, 20-26, and 53 results from the fact that while the specification teaches that there are three domains of Drosophila labial IRES which were demonstrated to have an effect on IRES activity, the specification does not teach the characteristics of the structure of domains I-III such that an artisan knows how to identify the three domains of any labial or Homeobox A IRES family member and know

that certain mutations in these three domains result in specific changes in IRES activity. For this reason, the examples taught in the specification do not provide guidance to the artisan to practice the claimed invention for the whole genus of labial/Homeobox A IRES family member. Therefore, the rejections of claims 1-5, 12-14, 17, 20-26, and 53 are maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40, 41, 43, and 45 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Mlodzik, et al. (1988, The EMBO Journal, 7: 2569-2578) as evidenced by Technical Services, 1993, Promega Catalog, see NCBI printout, gi number: 58196.

Claim 40 is broadly written that in addition to encompassing a vector that expresses a bicistronic nucleotide sequence, the claim encompasses a vector that is comprised of two cistrons which are not necessarily bicistronic.

Mlodzik et al. teach that the λF24 clone was isolated from a Drosophila genomic library. Mlodzik et al. teach that λF24 was mapped to chromosomal band 84A within the ANT-C. Mlodzik et al. teach that in situ hybridization analysis were performed in balanced deficiency (Df) chromosomes of the ANT-C region. Mlodzik et al. teach that their region mapped outside of the deficiency region of Df(3R)Scr and near the region

$Df(3R)Scx^{W+RX2}$. The labial gene behaves identically to these deficiencies. Thus, λF24 corresponded to labial (Mlodzik et al., page 2570, parag. under "Isolation and cytological mapping of genomic clones). Mlodzik et al. also teach that a cDNA clone of labial comprising the complete 3' end and a large portion of the 5' exon was obtained from a library provided by L. Kauvar (Mlodzik et al., page 2571, 2nd col., parag. under "Structure and sequence of the F24 gene"). Mlodzik et al., in Figure 4 teach that nucleotide sequence and deduced amino acid sequence of the clone. The clone contains a 5' UTR, which when compared to a sequence search, is the IRES of labial. The IRES of labial, shown in figure 4, is operably linked to one cistron, labial. Mlodzik et al. teach that genomic or cDNA fragments isolated from phage DNA was usually subcloned into pGEM vectors or Bluescript vectors (Mlodzik et al., page 2577, Materials and Methods, under "DNA and RNA methods"). According to the information posted on NCBI by Promega, the pGEM vector comprises an ampicillin resistance gene.

Mlodzik et al. anticipate claims 40, 41, 43, and 45 as the pGEM vector comprising genomic labial (e.g. sequence of Figure 4) would be comprised of at least two cistrons (labial and ampicillin) and at least one nucleotide sequence that provides IRES activity operably linked to at least one of said at least two cistrons, wherein the nucleotide sequence that provides IRES ativity comprises a nucleotide sequence comprising SEQ ID NO. 1.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER